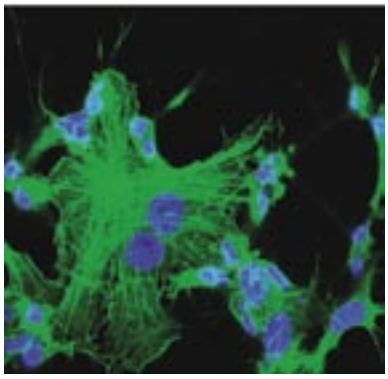
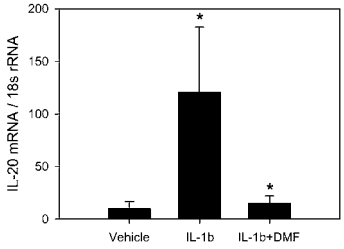


Silencing Spurs Survival

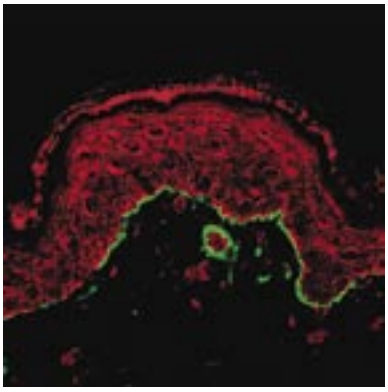
Although activation of the MAPK signaling pathway contributes to oncogenesis in many cancers, it may be a negative selection factor for Merkel cell carcinoma (MCC). As recognized so far, UISO cells are the only MCC cells in which MAPK signaling is preserved. When Houben and co-workers activated the MAPK pathway in UISO cells by inducing a form of the c-Raf-1 kinase domain, it led to morphologic changes, loss of actin stress fibers, and apoptosis. Because these effects could be prevented with the MEK-specific inhibitor U0126, this provides new perspectives on potential therapeutics for MCC using Raf-activating pharmacologic agents. ***See page 2116***

Will the Active Fumarate Step Forward?



To investigate the effect of fumaric acid esters on the p38 MAPK signaling pathway and mitogen and stress-activated kinases 1 and 2 (MSK1/2), Gesser and co-workers incubated normal cultured human keratinocytes with one of three fumaric acid esters: dimethylfumarate (DMF), methylhydrogen fumarate (MHF), or fumaric acid (FA). Cultures were then stimulated with interleukin-1 (IL-1) before kinase activation was assessed. Both MSK1 and -2 activations were significantly inhibited after pre-incubation with DMF and stimulation with IL-1, but MHF and FA had no effect. These study results identify DMF, when compared with MHF and FA, as the pharmacologically active compound in the treatment of psoriasis. ***See page 2129***

Epidermal Opioid Systems and Pruritus in AD



To investigate the distribution of the κ-opioid system in human epidermis and the opioids' association with peripheral itch, Tominaga and colleagues analyzed cultured keratinocytes and normal human skin samples. In skin biopsies from healthy volunteers compared with those from patients with atopic dermatitis (AD) before and after PUVA therapy, the κ-opioid system was downregulated in the epidermis of AD patients. These data suggest that the balance between μ- and κ-opioid systems may be involved in the modulation of peripheral itch sensation, with the μ-opioid system being itch inducible and the κ-opioid system itch suppressive. These studies expand the knowledge of itch control and suggest new approaches for the development of peripherally acting opioid antipruritics with possibly fewer or no central side effects. ***See page 2228***

Dandruff Gene

DeAngelis *et al.* report on a *Malassezia*-mediated lipid metabolic process likely involved in the etiology of dandruff and seborrheic dermatitis. Lipase activity was detected in four species of *Malassezia,* including *M. globosa,* which is commonly found on the human scalp. The investigators purified diglyceride-hydrolyzing lipase from isolated *M. globosa* cellular extract and performed peptide sequencing. The corresponding lipase gene *(LIP1)* was then cloned and sequenced. Expression was detected on three of five human scalps. ***See page 2138***

Gluten-Free Diet and IL-8

Hall *et al.* showed that when patients with dermatitis herpetiformis with elevated serum levels of interleukin-8 (IL-8) maintain a gluten-free diet, IL-8 levels normalize with an associated reduction in the levels of intestinal mucosal IL-8 mRNA expression and serum IgA antitissue transglutaminase antibodies. This suggests that gastrointestinal inflammation may create a "pro-inflammatory" profile in circulating inflammatory cells that, when accompanied by a minor elevation in local cytokines, may lead to significant local inflammation. This may be an important mechanism in the development of other skin diseases associated with gastrointestinal inflammation and other organs such as the joints. ***See page 2158***

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